Canine Mast Cell Tumors

By: Dr. Custead

WVRC
Introduction

- Mast cells
  - Resident inflammatory cell of the skin, lungs, gastro-intestinal tract
  - Reactions secondary to IgE binding
  - Allergic reactions
  - Granules contain:
    - Histamine
    - Serotonin
    - Heparin
    - Vasoactive amines
    - Others
Introduction

• Most common cutaneous tumor in the dog
• Second most common cutaneous tumor in the cat

• Predisposed breeds:
  – Boxers, Boston Terriers, Labrador Retrievers, Beagles, Shar-Pei and Schnauzers
  – Boxers tend to have a more favorable prognosis
    • Boston Terriers too?
  – Shar-Pei have a worse prognosis
Diagnosis

• The great pretender
• ALL cutaneous tumors should be aspirated 1st
  – Prior to surgical removal of incisional/excisional biopsy
• Other round cell tumors?
• Special stains?
  – Toluidine blue
  – Geimsa
“The Great Pretender”

- Solitary skin tumor
- Multiple skin lesions
- Dermal
  - 1 - 10 cm
  - Well-circumscribed, raised
  - Ulceration
- Subcutaneous
  - Soft, ill-defined mass
  - Normal overlying skin
  - May be confused with a lipoma
# Natural History

<table>
<thead>
<tr>
<th><strong>Good Guys</strong></th>
<th><strong>Bad Guys</strong></th>
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</thead>
<tbody>
<tr>
<td>Small</td>
<td>Large</td>
</tr>
<tr>
<td>Slow growing</td>
<td>Older dog</td>
</tr>
<tr>
<td>Right breed</td>
<td>Wrong breed</td>
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<tr>
<td>Subcutaneous</td>
<td>Quick growing</td>
</tr>
<tr>
<td>Good location</td>
<td>Ulcerated</td>
</tr>
<tr>
<td>LOW GRADE</td>
<td>Wrong location</td>
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<tr>
<td></td>
<td>HIGH GRADE</td>
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</tbody>
</table>
Natural History

Good Guys
Surgically cured

Bad Guys
Risk of local & distant metastasis

Sites of Metastasis:
Regional lymph nodes,
liver, spleen,
bone marrow
Rarely lungs
QUESTIONS
Complications

- Gastro-intestinal ulceration
  - 35-83% of cases
  - Increased histamine
- NOT related to:
  - Grade
  - Stage
  - Tumor size
- Decreased gastrin
Complications

• Hypotensive events
  – Histamine associated
    • Via smooth muscle H1 receptors
  – Less characterized vasoactive substances
    • Prostaglandin D?
Complications

• Arrhythmias - can be life threatening
  – Cardiac H1 and H2 receptors
  – Often secondary to rapid cell kill
    • Hyperthermia, cryosurgery or aggressive manipulation of large tumors
Complications

- Post-op delayed wound healing
  - Secondary to local release of
    - Histamine
      - Binds to macrophage receptors
      - Fibroblast suppressor factor
    - Proteolytic enzymes
  - Heparin
    - Coagulation abnormalities
    - More common in larger tumors, > 3 cm
QUESTIONS
Prognostic factors

- **HISTOLOGIC GRADE**
- Mitotic rate
- Clinical Stage
- Location
  - Preputial, scrotal, subungual, oral, mucosa
  - Note: inguinal/perineal
- Growth rate
- Recurrence

- Systemic signs
- Breed
- Tumor size
- C-Kit mutation
- Ki-67
  - <1.8
  - >1.8
- AgNOR
  - Was as or more predictive of behavior than grade
- PCNA
BIOPSY PRIOR TO DEFINITIVE SURGICAL REMOVAL
Pathology

3 Grades
(Patnaik Grading System)

» I or low grade
» II or intermediate grade
» III or high grade

Low vs High Grade
(2-Tier Grading System)

» Low vs high
Cons of Patnaik Grading System

• Subjective grading system
  – Northrup et al., 2005
  • 60 MCT evaluated (20 tumors of each grade)
  • 10 pathologists (blinded)
  • Only 4/60 tumors did all pathologists agree on grade
  • 10% (6/60) tumors were assigned all three grades

Cons of Patnaik Grading System

• Majority (>70%) of MCT are assigned to grade II
• Significant variability exists in behavior among grade II MCT
  – Garden-variety (i.e. cured with surgery alone)
  – More aggressive (require therapy beyond surgery)

Kiupel et al. Vet Pathol. 2011
Has it Already Spread?

Should I stage before or after a biopsy?
The diagnostics you’ll want to do will be dependent on prognostic factors.
Staging

- CBC/chemistry profile
- Urinalysis
- Abdominal radiographs
- +/- Thoracic radiographs
  - If tumor is cranial to diaphragm
  - Confirm lack of presence of other pathology
- Regional lymph node aspirates
- Aspirates of all cutaneous masses
- +/- Bone marrow aspirate
Stages

- **Stage 0**
  - One tumor incompletely excised from the dermis, N0

- **Stage 1**
  - One tumor confined to the dermis, N0

- **Stage 2**
  - One tumor confined to the dermis, N1

- **Stage 3**
  - Multiple dermal tumors or large infiltrating tumor with or without regional LN involvement

- **Stage 4**
  - Any tumor with M or recurrence with metastasis
Metastatic Rate

- **LOW GRADE**
  - <10%

- **LOW-MODERATE GRADE**
  - 15%

- **HIGH GRADE**
  - 55-96% (~80%)

- **Visceral form**
  - MST = 90 days
TREATMENT DEPENDS ON BIOLOGICAL BEHAVIOR

(i.e. grade)
With any treatment, never prescribe more treatment than necessary to control the cancer
COMPLETE surgical removal is imperative to improve long-term outcomes in dogs with cutaneous mast cell tumors, regardless of grade.
High Grade

• Wide surgical excision
  – 3 cm margins (greater?)
  – 2 cm margins?
  – One facial plane

• Curative surgical intent with dirty margins
  – Surgical revision vs RT

• Systemic Treatment
  – High grade
  – Intermediate grade
Low Grade

• SURGICALLY CURRED

• Narrow surgical margins (1-2 cm)
  – Especially if small

• Incomplete or narrow surgical margins
  – RT, chemotherapy or monitoring
Mass on extremity

- Narrow margins expected
- **Low** (or intermediate grade)
  - 30% will recur with dirty margins
  - More local treatment depends on owner
  - **MONITOR** vs RT
    - RT: 2 year control = 85-95% (low to intermediate)
- High grade
  - **Requires** more local treatment
Intermediate grade

- 50-75% cured with surgery
- 5% will recur, up to 15% will metastasize

What to do to better determine behavior?

**Ask pathologist to use High/Low Grading System**

- What is the MI?
- Special stains
  - (PCNA, AgNOR, Ki-67, c-Kit)

Rigorous recheck schedule

- 1 month after Sx
- Every 3 months for 1.5 years
- Every 6 months thereafter

Berlato. et al. VCO. 2015
Systemic therapy

• Vinblastine (#8) + Prednisone
  – 4 treatments, weekly, then 4 treatments, every other week
  – Prednisone (2mg/kg initially, tapered)
  – After Sx - MST - not reached, 1374 days (high)
  – After Sx + RT - MST
    • High grade = 3.8 years
    • Intermediate = 100% alive at 2 years

• CCNU, Vinblastine, Cytoxan, Hydroxyurea and Vinorelbine

• Toceranib Phosphate
  – ~70% chance of response if c-kit +
  – ~30% chance of response if c-kit -

Copper, et al. VCO. 2009
Rassnick, et al. VCO. 2010
Vickery, et al. VCO. 2008
London et al. AACR. 2009
Research in the future will likely more definitively show that combinational systemic therapy will improve outcome over single-agent protocols.
Ancillary Therapy

- Use whenever there is evidence of residual disease or high risk of degranulation
  - Dirty microscopic margins
  - Gross disease
  - Undergoing aggressive resection or systemic therapy

- Diphenhydramine (2-4 mg/kg PO TID) - H1
- Famotidine (0.5 – 1.0 mg/kg PO BID) - H2
- Omeprazole (1 mg/kg PO BID)
- Sucralfate
Pearls of Wisdom

• More than one tumor
  – 11-14%

• Most common location
  – Trunk

• Least common
  – Head and neck

• DISSEMINATED mastocytosis
  – In the dog ALWAYS preceded by a mass

“The surgery went well. It had spread, but I’m quite confident we got it all.”
Works Cited

• Cancer in Dogs and Cats, Medical and Surgical Management. by Morrison

• Small Animal Clinical Oncology. By Withrow and MacEwen, 4th Edition

• Tons of papers 😊